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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,851	09/19/2003	Peter Bodine	00630/100M091-US2	6790

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,851	BODINE, PETER	
	Examiner	Art Unit	
	XIAOZHEN XIE	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-21 and 24-43* is/are pending in the application.

4a) Of the above claim(s) *7-19 and 26-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,20,21,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment of the claims filed on 11 July 2008 has been entered.

Claims 5, 22 and 23 have been cancelled. Claims 1-4, 6-21 and 24-43 are pending. Claims 7-19 and 26-43 are withdrawn from further consideration as being drawn to a nonelected invention. Claims 1-4, 6, 20, 21, 24 and 25 are under examination.

Specification

The disclosure remains objected to because the first line of the specification fails to include updated cross-reference to related applications. Specifically, the Application No: 10/169,545 is now patented.

Applicant argues that the first line of the specification was previously updated to reflect that Application Serial No. 10,169,545 is now U.S. Patent No. 7,098,372. Applicant further directs to U.S. Patent Application No. 2008/0166356. However, upon further review, there is no record in the prosecution history, or in the U.S. Patent Application No. 2008/0166356, indicating such update.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20, 21 and 24 remain rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for: *a pharmaceutical composition comprising an antibody generated using the sFRP-1 of SEQ ID NO: 2, or using a fragment thereof comprising the amino acids 217-231 of SEQ ID NO: 2, as an immunogen, wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, and wherein the antibody promotes bone-forming activity in a mammal,* does not reasonably provide enablement for pharmaceutical compositions comprising antibodies generated using any portions of sFRP-1. The amended claims 1-4 and 6 are also included in this rejection. The basis of this rejection is set forth in the previous office actions and the following.

Applicant argues that claim 20 has been amended to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunogen." Applicant argues that the amended claims are fully enabled for generating an antibody using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunogen, including the specified fragment recited in claim 24. Applicant argues that amendment has obviated the rejection under 35 U.S.C. § 112, first paragraph.

Applicants' argument has been fully considered but has not been found to be persuasive.

The claim recitation of "at least one antibody generated using ***a*** secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunogen", still reads on antibodies

generated using fragments of sFRP-1 protein of SEQ ID NO: 2, i.e., fragments of any portions and lengths of SEQ ID NO: 2. The claim requires that "wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1". As stated previously, the specification does not provide sufficient support that antibodies generated using any portion of sFRP-1 can have the specific antigen binding activity and exhibit the recited inhibitory activity. While the specification discloses that antisera generated using the peptide of amino acids 217-231 of sFRP-1 as an immunogen inhibited cell death mediated by overexpression of this gene, the specification, however, has not provided support for antibodies generated using any fragment of sFRP-1 exhibiting the required activity and to be able to function in a pharmaceutical setting.

The amended claims 1-4 and 6 are also included in the rejection for the same reason because claim 1 has been amended to recite "wherein the antibody promotes bone-forming activity in a mammal". Claim 1 encompasses antibodies "generated using ***a*** secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunigen", which reads on antibodies generated using fragments of sFRP-1 protein of SEQ ID NO: 2, i.e., fragments of any portions and lengths of SEQ ID NO: 2. The specification does not provide sufficient support that antibodies generated using any portion of sFRP-1 can promote bone-forming activity in a mammal. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification. It required undue experimentation for one skilled in the art would not know how to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The amended claims 20, 21 and 24 remain rejected under 35 U.S.C. 102(e) as being anticipated by Umansky et al. (U. S. Patent No: 6,433,155 B1, which was filed on 24 September 1997), for reasons of record set forth in the previous office actions.

Applicant argues that claim 20 has been amended to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunogen and wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: I." Applicant argues that the SARP proteins described by Umansky et al. are not identical to the sFRP-1 protein of SEQ ID NO: 2, and thus, antibodies generated using Umansky's protein or fragments thereof, will be different from the claimed antibodies. Applicant argues that even though there is a region of identity between Umansky's SARP protein and SEQ ID NO: 2 (i.e., amino acids 217-231), claim 24 requires that the antibody is generated using at least this fragment as an immunogen and is also capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1. Applicant argues that Umansky et al. provide no teaching or suggestion with regard to the unexpected

property of the claimed pharmaceutical compositions comprising the claimed antibodies for regulating bone-forming activity in a mammal, and do not teach an antibody with the property that it is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1.

Applicants' argument has been fully considered but has not been found to be persuasive.

The claims still read on antibodies generated using fragments of sFRP-1 (see *supra*), and the claims encompass "at least one antibody generated using a sFRP-1 of SEQ ID NO: 2". Umansky et al. teach a pharmaceutical composition comprising an antibody against a polypeptide of SARP, e.g., SARP-2, also known as sFRP-1. The polypeptide of SARP-2 shares a 99.7% similarity to the SEQ ID NO: 2 of the instant application, and has 100% identity in the amino acid sequence of residues 217-231. Umansky et al. teach that the antibody includes polyclonal and monoclonal antibodies. Given the similarity between SARP-2 and the instant SEQ ID NO: 2 (i.e., 99.7% homology and 100% identity in the amino acid sequence of residues 217-231), one of ordinary skill in the art would recognize that a substantial population of the antibodies encompassed by the prior art would be identical to the instant antibodies.

While Umansky et al. do not expressly teach that the antibodies are capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, this activity would reasonably be considered to be inherent to the antibodies. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

The amended claims 20, 21 and 24 remain rejected under 35 U.S.C. 102(e) as being anticipated by Rubin et al. (U. S. Patent No: 6,479,255 B1, which has a priority date on 29 May 1997), for reasons of record set forth in the previous office actions.

Applicant argues that claim 20 has been amended to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2 as an immunogen wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: I", and claim 24 recites that the antibody is generated using at least a specific base fragment of sFRP-1 protein of SEQ ID NO: 2 and is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: I. Applicant argues that the FRP protein described by Rubin et al. is not identical to the sFRP-1 protein of SEQ ID NO: 2, and since claims 20 and 24 require the use of a sFRP-1 of SEQ ID NO: 2 as an immunogen, Rubin et al. cannot anticipate the pending claims. Applicant argues that Rubin et al. do not teach an antibody that is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1.

Applicants' argument has been fully considered but has not been found to be persuasive.

The claims still read on antibodies generated using fragments of sFRP-1 (see *supra*), and the claims encompass "at least one antibody generated using a sFRP-1 of SEQ ID NO: 2". Rubin et al. teach anti-FRP antibody compositions with polyepitopic and monoclonal specificity and their pharmaceutical uses (col. 8, lines 18-23; col. 18, lines

21-32). Rubin et al. teach antibodies raised against full-length or an epitope of FRP polypeptide (col. 14, lines 45-64). The amino acid sequence of the FRP taught by Rubin et al. has 96.5% local similarity to SEQ ID NO: 2 of the instant application, and has 100% identity in the amino acid sequence of residues 217-231. Given the similarity between the FRP and the instant SEQ ID NO: 2 (i.e., 96.5% homology and 100% identity in the amino acid sequence of residues 217-231), one of ordinary skill in the art would recognize that a substantial population of the antibodies encompassed by the prior art would be identical to the instant antibodies.

While Rubin et al. do not expressly teach that the antibodies are capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, this activity would reasonably be considered to be inherent to the antibodies. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

The amended claims 1, 3, 4, 6, 20, 21, 24 and 25 remain rejected under 35 U.S.C. 102(e) as being anticipated by Rubin et al. (US 2003/0175864 A1, which has a priority filing date on 29 May 1997), for reasons of record set forth in the previous office action.

Applicant argues that claim 1 has been amended to recite "wherein the antibody promotes bone-forming activity in a mammal", and claim 20 has been amended as described above. Applicant argues that Rubin et al. do not teach an antibody with the property of inhibiting cell death mediated by overexpression of the polynucleotide set

forth in SEQ ID NO: 1, and do not teach a pharmaceutical composition containing such an antibody with the property of regulating bone-forming activity in a mammal.

Applicants' argument has been fully considered but has not been found to be persuasive.

Rubin et al. teach anti-FRP antibody compositions and their pharmaceutical uses [0058] [0107]. Rubin et al. teach the antibodies raised against full-length recombinant FRP polypeptide which has the identical amino acid sequence to the SEQ ID NO: 2 of the instant application [0090]. Rubin et al. also teach the polynucleotide sequence encoding the FRP protein. Although the polynucleotide sequence is not identical to SEQ ID NO: 1 of the instant invention, the expression product, however, is identical. With respect to the properties of the antibodies, i.e., inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, and being capable to regulate bone-forming activity in a mammal, these function/activities would reasonably be considered to be inherent to the antibodies. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin et al. (US 2003/0175864 A1), in view of Chan et al. (J. Biol. Chem., 1992, 267(35):25202-25207), for reasons of record set forth in the previous office action.

Applicant argues that Chan describes rat Fz-1 and Fz-2 proteins and provides comparisons with the *Drosophila* protein and merely hypothesizes about the general nature of mammalian Fz proteins. Applicant argues that Chan provides no teaching with respect to a human protein of SEQ ID NO: 2 from human osteoblast cells. Applicant argues that claim 1 has been amended to recite "an antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen, wherein the antibody promotes bone-forming activity in a mammal", and dependent claim 2 further specifies that the sFRP-1 is from human osteoblast cells, and that nothing in Rubin or Chan provides a teaching or motivation, much less the expectation of success for making the claimed pharmaceutical composition comprising an antibody with the property of promoting bone-forming activity in a mammal.

Applicants' argument has been fully considered but has not been found to be persuasive.

The Rubin et al. reference teaches all limitations recited in the claims, including the amino acid sequence of sFRP-1 of SEQ ID NO: 2, except that the FRP protein is from human osteoblast cells (claim 2). Chan et al. cures the deficiency by teaching that the homologs of the *Drosophila* gene, *frizzled (fz),* are widely expressed in mammalian tissues, such as osteoblasts. Chan et al. detected the gene from rat, as well as from human and mouse (pp. 25205, col. 1, bottom paragraph). Therefore, it would have been

prima facie obvious to one of ordinary skill in the art at the time the invention was made to use an FRP protein isolated from human osteoblast cells for generating an anti-FRP antibody. One of ordinary skill in the art would have been motivated to do so, because Chan et al. teach that the *fz* gene homologs are present in rat, human and mouse, and mammalian tissues, in particular osteoblasts, contain such proteins. Therefore, the combined teachings provide a reasonable expectation of successfully preparing the composition.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
October 14, 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646